



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/950,051 | 09/12/2001 | Edouard Yeramian | 03495.0209 | 8676 |

7590 03/16/2005

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.
1300 I STREET, N.W.
WASHINGTON, DC 20005-3315

EXAMINER

SMITH, CAROLYN L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/950,051

Applicant(s)

YERAMIAN, EDOUARD

Examiner

Carolyn L Smith

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) 2 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-6 is/are rejected.
- 7) ☒ Claim(s) 1 and 3-6 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> . |

Continuation of Attachment(s) 6). Other: Petition for colored drawings granted.

Art Unit: 1631

DETAILED ACTION

Applicant's election of Specie A (stability curve analysis which involves the detection of genetic signals which are the disruption of the double-helix), filed 11/30/04, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claim 2 is withdrawn as being drawn to a non-elected specie.

The title of the invention is not short and descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to genes and the physics of the DNA double helix, formulation of a physics-based gene identification method, ab initio identification of genes in eukaryotic genomes, whereas in contrast the elected claims are specifically directed to a method for the identification of genes and genetic signals.

The petition for colored drawings, filed 2/25/02, is granted.

Claims herein under examination are 1 and 3-6.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 8 (lines 16-17) of the specification and pages 2 (line 13) and 3 (lines 12-13) of the preliminary amendment, filed 2/25/02. Applicant is

Art Unit: 1631

required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 1 is objected to because of the following informality: Claim 1 (line 8) contains a comma that appears to be grammatically incorrect. Correction is suggested by removing this comma.

Claims 3-6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 3-6 recite intended uses that do not further limit the method steps of claim 1.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 3-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1 and 3-6 are directed to a gene identification method apparently comprising a series of mathematical steps for data manipulation, equivalent to mental processes. Applicant is reminded that mental processes are not statutory subject matter under 35 USC 101.

Art Unit: 1631

The claimed method is not restricted to be a computer-implemented method; however, the specification indicates that the method is intended to be one implemented by a computer. In the event that the claimed method steps are implemented by a computer, the method claims are not statutory as any computer implemented method must produce a result that is concrete, tangible, and useful. As set forth in MPEP 2106.IV.B:

“In practical terms, claims define nonstatutory processes if they:

- consist solely of mathematical operations without some claimed practical application

(i.e., executing a “mathematical algorithm”); or

- simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30

USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31

USPQ2d at 1759), without some claimed practical application.”

As set forth in MPEP 2106.II.A :

The claimed invention as a whole must accomplish a practical application. That is, it must produce a "useful, concrete and tangible result." State Street, 149 F.3d at 1373, 47 USPQ2d at 1601-02. The purpose of this requirement is to limit patent protection to inventions that possess a certain level of "real world" value, as opposed to subject matter that represents nothing more than an idea or concept, or is simply a starting point for future investigation or research (Brenner v. Manson, 383 U.S. 519, 528-36, 148 USPQ 689, 693-96); In re Ziegler, 992, F.2d 1197, 1200-03, 26 USPQ2d 1600, 1603-06 (Fed. Cir. 1993)).

As set forth in MPEP 2106.IV.B.2(b) (ii):

“A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible and useful. See AT &T, 172 F.3d at 1358, 50 USPQ2d at 1452. For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory.

Art Unit: 1631

There does not appear to be any actual result produced by this method. Analysis is performed but there is no result of genetic signals or genes being identified. Since, there is no apparent result, the invention is not concrete, tangible, and useful. Because, the claimed method does not produce a concrete, tangible and useful result, claims 1 and 3-6 do not recite statutory subject matter.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The preamble of claim 1 recites a method for identifying genes and genetic signals; however, no actual identification takes place in the method steps. Therefore, it is unclear if the preamble or the body of the claim controls the metes and bounds of the instant claim.

Clarification of the metes and bounds of the claim via clearer claim wording is requested.

Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 (lines 1-2 and 10) recites the phrase “based on” which is vague and indefinite. It is unclear what parameters and to what degree these parameters must be met to be considered to

Art Unit: 1631

be “based on”. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1, step (a), recites “using the classical physical model of helix-coil transitions” is vague and indefinite. It is unclear what step is intended by Applicant for using such a classical physical model of helix-coil transitions. The specification (paragraphs 007, 012, and Figure 1) mentions using SIMEX to perform the structural calculations (helix coil model) as well as Pade Laplace methods, but it is unclear if step (a) of claim 1 is used to determine steps (b) through (e) or if some other use of the model is intended. Clarification of this issue via clearer claim wording is requested. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 (line 5) contains two commas that create unclarity in the claim. By having commas in between the phrase “along a given sequence”, it is unclear if this phrase is therefore considered to be optional. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 (line 12) recites the phrase “donor/acceptor” which is vague and indefinite. It is unclear if the structural information must have only one of a donor or an acceptor or a combination of both. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 (line 12) recites the phrase “in correspondence with” which is vague and indefinite. It is unclear what parameters and to what degree these parameters must be met to be

Art Unit: 1631

considered to be “in correspondence with”. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 recites the limitation "the linear DNA" in line 6. There is insufficient antecedent basis for this limitation in the claim as there is no prior mention of linear DNA. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 1 (line 12) recites the phrase “the frontiers” which is vague and indefinite. The meaning of this phrase is unclear. Is this phrase referring to a border? Is this phrase referring to certain sections of the curves, and if so, which portions? Clarification of the metes and bounds of this phrase via clearer claim wording is requested. Claims 3-6 are also rejected due to their direct or indirect dependency from claim 1.

Claim 3 recites the limitation "the annotation" in line 2. There is insufficient antecedent basis for this limitation in the claim. Correction is suggested by amending the word “the” to “an”.

Claim 6 recites the limitation "the genome" in line 1. There is insufficient antecedent basis for this limitation in the claim as the claim from which it depends mentions various genomes. Therefore, it is unclear which genome is being referred to in claim 6. Correction is suggested by amending the word “the” to “an”.

Art Unit: 1631

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Gotoh (Advances in Biophysics, Volume 16, pages 1-52, 1983).

Gotoh discloses the double-helical structure of DNA is disrupted into single-stranded random coils by heat (page 1, first paragraph). Gotoh discloses the study of helix-to-coil transition, or melting of DNA in various fields including physics (page 1, first paragraph), as stated in step (a) of instant claim 1. Gotoh discloses the double-to-single strand transition is called thermal denaturation or melting (page 3, first paragraph). Gotoh discloses measurement and theory of DNA melting enable comparisons of calculated (ab initio) with measured profiles for known-sequenced DNA species or restriction fragments (page 1, third paragraph). Gotoh discloses the ability to evaluate the stability of individual base pairs in DNA and estimating the probability of each base pair being in an open (unbound) state thus creating stability map and base-pair opening profiles (page 2, first paragraph; page 6, fifth paragraph; page 7, last paragraph; page 14, last paragraph to page 15, first paragraph) as well as melting profile equation (1) and curve (Figures 1 and 5 and page 3, last paragraph), which represent calculating stability curves, as stated in step (b) of instant claim 1. Gotoh discloses these profiles provide

Art Unit: 1631

information about roles of specific regions in various biologically important processes (page 2, first paragraph). Gotoh discloses the ordered structure of double stranded DNA is disrupted to a single strand (linear) state with an increase in temperature which can be monitored by various chemical, physicochemical, and biological assays (page 3, first and second paragraphs and Figure 1), as stated in step (c) of instant claim 1. Gotoh discloses Figure 1 and " $1-\Phi T$ " in equation 1 is made proportional to the fraction of base-pair doublets that have been disrupted after corrections for thermal expansion (page 4, first paragraph) which represents an analysis of stability curves for detecting genetic signals, wherein the genetic signals are the disruption of the double helix, as stated in step (d) of instant claim 1. Gotoh discloses the melting profiles of many DNA species have been measured including whole genomes (page 4, second paragraph; page 24, second paragraph; and Figure 1) which represents genetic signals of various genomes, as stated in instant claim 5. Gotoh discloses the use of various algorithms to study the melting of DNA (page 4, last paragraph to page 5, first paragraph). Gotoh discloses generating nucleotide sequence and parameter values as well as melting profiles on computer programs (page 16, second and third paragraphs). Gotoh discloses that in mammalian mitochondria some tRNAs recognize all four codons that differ by the third letter, whereas others recognize only such codons that allow either Watson-Crick or wobble base pairing at the third position (page 27, last paragraph) wherein the mammalian sample represents a eukaryotic genome, as stated in instant claim 6. Gotoh discloses that the recognition pattern may be correlated with the stability of codon-anticodon complexes (page 27, last paragraph). Gotoh discloses shifts of a renaturation curve from a melting curve to low temperature side (page 29, fourth paragraph). Gotoh discloses profiles with identified promoters and regulatory sites, terminator sites, origins of replication,

Art Unit: 1631

and genes in Figure 16. Gotoh discloses using hysteresis analysis to locate CMRs (cooperatively melting regions) on a DNA molecule (page 29, last paragraph), rates of denaturation and relaxation times, and theoretical (ab initio) and experimental profiles for restriction fragments isolated from the *E. coli lac* promoter-operator region (page 35, paragraphs 1-4), as stated in instant claim 4. Gotoh discloses that if the whole nucleotide sequence is known, it is possible to predict the thermolabile regions on a DNA molecule by calculating probability profiles (page 38, last paragraph). Gotoh discloses the theoretical (ab initio) approach allows accurate prediction of thermolabile regions to the level of a single base pair, so they are compared to various functional sites identified on the sequence (page 38, last paragraph to page 39, first paragraph). Figure 15 (its caption and page 40, third paragraph; page 42, third paragraph) discloses a thermal stability map and base-pair opening profile of Φ X174 DNA covering the full genome size as well as marker sites for mRNA startpoint and terminator site with genes indicated between the two maps, which represent the analysis of structural information of donor/acceptor sites, start and codon stops in correspondence with frontiers identified in the stability curve and open reading frame analysis for identifying genes, as stated in optional step (e) of instant claim 1 as well as the annotation procedure, as stated in instant claim 3. Gotoh discloses frequently opening regions (FORs) (page 40, third paragraph to page 41, first paragraph). Gotoh discloses relations between early melting regions, low stability regions, and functional loci (page 40, third paragraph and page 41, last paragraph). Gotoh discloses gene boundaries falling on or close to CMRs of various genomes (page 42, first paragraph).

Thus, Gotoh anticipates claims 1 and 3-6.

Art Unit: 1631

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al. (Progress in Biophysical and Molecular Biology, 1992, Volume 58, pages 225-257) supported by the Life Science Dictionary (1998).

Cheng et al. disclose the underlying stability of nucleic acid associations determines the molecular biology of genetic regulation and expression (page 225, lines 1-2) wherein the regulation and expression represent identification of genetic signals. Cheng et al. disclose the stability of double-stranded nucleic acids refers to helix-coil transitions that are characterized by physical and chemical techniques (page 226, first full paragraph) which represent using a classical physical model of helix-coil transitions, as stated step (a) of instant claim 1. Cheng et al. disclose using models, simulations, and theories (page 225, first paragraph). Cheng et al. disclose temperature affects duplex nucleic acid stability (page 226, first full paragraph). Cheng et al. disclose the use of melting curves study methods to probe the stability of oligo-duplexes by creating temperature induced transition (melting) profiles to evaluate various delta parameters involving temperature using algorithms (1) and (2) (page 226, last paragraph) which represents calculating stability curves involving probabilities of opening denatured double stranded DNA (see melting definition from Life Science Dictionary (see attached definition), as stated in step (b) of instant claim 1. The temperature induced transition melting profiles mentioned above allows evaluation of thermodynamic parameters delta H, delta S, and delta G (page 226, last paragraph) which represents determining disruption in the linear DNA for different temperatures as well as an analysis of stability curves for the detection of genetic signals, as stated in steps (c) and (d) of instant claim 1. Cheng et al. disclose α and C_T are the fraction of strands in the double stranded state and total strand concentration, respectively (page 226, last paragraph). Cheng et

Art Unit: 1631

al. disclose characterizing sequence dependence of base stacking for duplexes to predict the stability of a sequence (page 250, fourth paragraph). Cheng et al. disclose using theoretical techniques including molecular modeling, computer simulations, and free energy perturbation calculations to pursue structural and physical properties of duplexes (page 251, first full paragraph). Cheng et al. disclose using computational methods to interpret biological phenomena related to genetic studies (page 251, first full paragraph).

Thus, Cheng et al. anticipate instant claim 1.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Art Unit: 1631

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 8, 2005

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
3/10/05



UNITED STATES DEPARTMENT OF COMMERCE

U.S. Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

| | | | |
|---------------------------------|-------------|---|---------------------|
| APPLICATION NO./ CONTROL NO. | FILING DATE | FIRST NAMED INVENTOR / PATENT IN REEXAMINATION | ATTORNEY DOCKET NO. |
|---------------------------------|-------------|---|---------------------|

| |
|----------|
| EXAMINER |
|----------|

| | |
|----------|-------|
| ART UNIT | PAPER |
|----------|-------|

22605

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

The Petition to accept Color Drawings, filed 2/25/02, under 37 CFR § 1.84 (a)(2) is **GRANTED**.

Any inquiry concerning this Petition decision should be directed to Ardin Marschel, Ph.D., AU 1631 Supervisory Patent Examiner, whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

February 26, 2005
09/950,051

Ardin H. Marschel 2/26/05
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER